Early industry/HTA Collaboration: Can we afford not to do it?

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Pfizer Canada
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Current R&D Productivity is Alarming

Figure 2.6  Innovation Gap: R&D Investments Versus New Drug Approvals

PhRMA Member R&D Spending  New Drug Approvals (NMEs)

Source: Burrill & Company
### Scientific Advances: Can Innovation Master Master Complexity?

<table>
<thead>
<tr>
<th>Time</th>
<th>Key Developments</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 years ago</td>
<td>Disease of the blood</td>
</tr>
<tr>
<td>80 years ago</td>
<td>Understanding of leukemia and lymphoma as cancers</td>
</tr>
<tr>
<td>60 years ago</td>
<td>Chronic leukemia</td>
</tr>
<tr>
<td>Today</td>
<td>~38 leukemia types identified:</td>
</tr>
<tr>
<td></td>
<td>- Acute myeloid leukemia (~12 types)</td>
</tr>
<tr>
<td></td>
<td>- Acute lymphoblastic leukemia (2 types)</td>
</tr>
<tr>
<td></td>
<td>- Acute promyelocytic leukemia (2 types)</td>
</tr>
<tr>
<td></td>
<td>- Acute monocytic leukemia (2 types)</td>
</tr>
<tr>
<td></td>
<td>- Acute erythroid leukemia (2 types)</td>
</tr>
<tr>
<td></td>
<td>- Acute megakaryoblastic leukemia</td>
</tr>
<tr>
<td></td>
<td>- Acute myelomonocytic leukemia (2 types)</td>
</tr>
<tr>
<td></td>
<td>- Chronic myeloid leukemia</td>
</tr>
<tr>
<td></td>
<td>- Chronic myeloproliferative disorders (5 types)</td>
</tr>
<tr>
<td></td>
<td>- Myelodysplastic syndromes (6 types)</td>
</tr>
<tr>
<td></td>
<td>- Mixed myeloproliferative/myelodysplastic syndromes (3 types)</td>
</tr>
<tr>
<td>Today</td>
<td>51 lymphomas identified:</td>
</tr>
<tr>
<td></td>
<td>- Mature b-cell lymphomas (~14 types)</td>
</tr>
<tr>
<td></td>
<td>- Mature T-cell lymphomas (15 types)</td>
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<tr>
<td></td>
<td>- Plasma cell neoplasm (3 types)</td>
</tr>
<tr>
<td></td>
<td>- Immature (precursor) lymphomas (2 types)</td>
</tr>
<tr>
<td></td>
<td>- Hodgkin’s lymphoma (5 types)</td>
</tr>
<tr>
<td></td>
<td>- Immunodeficiency-associated lymphomas (~5 types)</td>
</tr>
<tr>
<td></td>
<td>- Other hematolymphoid neoplasm's (~7 types)</td>
</tr>
</tbody>
</table>

**INNOVATION**: Can we have more shots on goals?

**Oncology: Pfizer Programs**  
*(last 5 years)*

<table>
<thead>
<tr>
<th>Sunitinib MRCC</th>
<th>Sunitinib PNeT</th>
<th>Crizotinib NSCLC ALK+</th>
<th>Axitinib MRCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>A4021016 Figitumumab Metastatic lung cancer 1st line</td>
<td>A6181122: Colorectal Cancer</td>
<td>CAM Refractory Gastric cancer</td>
<td>A6181087 SUT Metastatic Lung cancer 2nd line</td>
</tr>
<tr>
<td>A6181077: phase 2 head to head in triple negative breast cancer</td>
<td>A3671009 TRE Metastatic Melanoma 1st line</td>
<td>CAM -Small Cell Lung cancer</td>
<td>A6181084 SUT Metastatic Lung cancer 1st line</td>
</tr>
<tr>
<td>CAM Adjuvant treatment of colorectal cancer</td>
<td>A6181120: Prostate Cancer</td>
<td>A6181170: Hepato-cellular Carcinoma</td>
<td>A4061028: Adeno-carcinoma of the pancreas</td>
</tr>
<tr>
<td>A4021018 Figitumumab Metastatic lung cancer 2nd line</td>
<td>A6181064: 1st line MBC</td>
<td>A6181099: 2nd line MBC</td>
<td>TLR-9 antagonist in Metastatic Lung cancer</td>
</tr>
<tr>
<td>TRE Metastatic Lung</td>
<td>TRE Met Colorectal</td>
<td>TRE Pancreatic cancer</td>
<td>CI-1033 Met Breast</td>
</tr>
<tr>
<td>Axitinib Metastatic Breast Cancer</td>
<td>CI-1033 Met Lung</td>
<td>Figitumumab MBC</td>
<td>Figitumumab Colorectal</td>
</tr>
</tbody>
</table>
Patients and Physicians Waiting for Treatments

- 8% of compounds entering Phase 1 will make it to market, down from 14% fifteen years ago

- Cost of development are escalating

- Failures due to lack of safety and/or efficacy

- Inability to predict failures

- Major barriers to address uncommon diseases and explore unproven technologies
<table>
<thead>
<tr>
<th>MOA</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Passive immunotherapy</td>
<td>MABT5102A (mAb; Genentech) GSK933776A (mAb; GSK) AAB-003 (Pfizer)</td>
<td>Ponezumab (PF-0360365 (mAb; Pfizer)</td>
<td>Bapineuzumab (AAB-001; JAI/Pfizer) IVlg 10% (IV human Immune Globulin; Baxter) Solanezumab (mAb; Eli Lilly)</td>
</tr>
<tr>
<td>Vaccines</td>
<td>V950 UB311 (vaccine; Pfizer) AFFITOPE AD03 (vaccine; Affiris)</td>
<td>ACC-001 (Conj.vaccine; JAI/Pfizer) CAD 106 (vaccine; Cytos/Novartis) AFFITOPE AD02 (vaccine; Affiris)</td>
<td>AN-1792 (Elan/Wyeth/Pfizer) semagacestat (γ-secretase inhibitor; Eli Lilly) Flurizan (Myriad)</td>
</tr>
<tr>
<td>Aβ Production Inhibition</td>
<td>GSI-953 (γ-secretase inhibitor; Pfizer) CTS21166 (β-secretase inhib CoMentis)</td>
<td>CHF-5074 (γ-secretase inhibitor; Chieis Pharma)</td>
<td></td>
</tr>
<tr>
<td>RAGE Inhibition</td>
<td>PF-0494700 (RAGE; Pfizer)</td>
<td>AZD-103/ELND005 (scyllo-inositol; Transition/Elan)</td>
<td></td>
</tr>
<tr>
<td>Aβ Aggregation Inhibitor</td>
<td>AZD3480 (NNR ag; AstraZeneca) SAM-760 (5HT4 anag; Pfizer) PF-04995274 (5HT4 anag; Pfizer) AZD1446 (NNR ag; AstraZeneca) LuAE58054 (5HT6 anag; Lundbeck) ABT-384 (unk; Abbott)</td>
<td>Rember (Tau aggre inhib) (NGF/adebovir; Ceregene) SAMM31 (5HT6 anag; Pfizer) SB742457 (5HT6 anag; GSK) MEM3454/R05313534 (NNR ag; Roche) TRx0014 (Tau; TauRx Therapeutics) HF0220 (steroid; Hunter-Fleming LTD)</td>
<td>Alzhemed (tramiprosate - Neurochem) Dimebon (Hist. antag+; Pfizer/Medivation) Lecozotan (5HT1A Agonist; Wyeth/Pfizer)</td>
</tr>
<tr>
<td>Other MOAs</td>
<td>LNK 754 (Farnesyl transf inhib; Link Medicine Corp) NRM8499 (tramiprosate prodrug Bellus)</td>
<td>CERE-110. (γ-secretase inhibitor; BMS) GSK-239512 (H3 ant; GSK) ST101 (unk; Sonexa) T-817MA (neurotrophic; Toyama) PF-04447943 (PDE10 inhibitor; Pfizer) TRx0014</td>
<td></td>
</tr>
</tbody>
</table>
What is the Real Value of Innovation?

Average % in a two-year period* of products with Full Listing Status (for two-year periods ending Aug. 2008 to Aug. 2011)

Each data point represents a two-year average
Impact on Clinical Development

2 Examples of Pfizer Developmental Programs

- Sulopenem: pneumonia
  - Development CEASED: lack of differentiation for payers
- PF-734: diabetes
Pharmaceutical Research and Development is Evolving

**PAST**
- Regulatory Need

**PRESENT**
- Regulatory Need
- Payer Need
Regulatory Review & Approval

Phase III
1,000–5,000 patient volunteers used to monitor adverse reactions to long-term use

Phase II
100–300 patient volunteers used to look for efficacy and side effects

Phase I
20–80 healthy volunteers used to determine safety and dosage

Preclinical Testing
Laboratory and Animal Testing

Discovery

Length of time in years

Generic Entry

Public Reimbursement

1. Aligned with the needs of the healthcare system. Horizon scanning of what society needs. Validate disease and pathways

2. Early Engagement with Payers

Sources:
Towards New Models of Collaboration

- “Ways need to be found to develop partnerships that link researchers, industry, governments, policy makers, and health system managers so that the fruits of innovation are quickly and appropriately taken into health systems and reach those that need them”.

Organisation for Economic Co-operation and Development
Translating Discoveries into New and Better Therapies

- ‘-omics’
- Understanding human physiology
- Imaging
- ICT

Public investment

Pre-competitive collaborative research

Private investment

Better understanding of disease/drug mechanisms

More efficient drug discovery and development

Better medicines, faster

Health benefits for patients

Understanding human physiology

Translating Discoveries into New and Better Therapies

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Translating Discoveries into New and Better Therapies

Understanding human physiology
Early Discovery

MaRS EXCITE

SGC
A public-private partnership that supports the discovery of new medicines through open access research.

Commercialisation of innovations from the UK National Health Service

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*Corresponding author

CQAM
Centre for Drug Research and Development

Pfizer
- Feedback prior to phase 3 lock
- Study design; comparator, endpoints, follow-up period, other data gaps

http://www.nice.org.uk/aboutnice/scientificadvice/AboutScientificAdvice.jsp
Ways that HTA Can Shape the R&D Process

Not *always* in the toolkit yet important

**Currently in the HTA toolkit:**
- Certainty of evidence and design of pivotal studies
  - Endpoint
  - Comparator
  - Follow-up
  - Generic QoL measures
- Economic evaluation and budget impact
- Patient/caregiver relevant outcomes and preferences
- Feasibility and health technology management plans
  (how to introduce and adopt the technology optimally)
- Further evidence gathering plans (phase 4)
- Burden of Disease
- Areas of unmet need
- Ethical considerations
- Labour workforce impact and productivity
In Conclusion...

- The R&D process is becoming more complex and risky.
- The few medicines coming out R&D need to meet society and payers needs.
- New models of collaboration between all stakeholders are being put in place to address the innovation gap.
- Such models are urgently required between the Biopharma sector and payers/HTA bodies.
- HTA has matured into a pivotal component of the R&D continuum.
- HTA has the potential to become ‘dynamic’, it can guide R&D, manage optimal adoption of health technologies, contribute to the knowledge base and act as a conduit for future innovations.